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The Role of the Anterior Cingulate in Automatic and Controlled Processes: A Developmental Neuroanatomical Study

Received 6 September 1995; revised 21 February 1996; accepted 29 August 1996

ABSTRACT: This study examines the role of the anterior cingulate in the development of attention. Task performance relying predominantly on either automatic or controlled processes was correlated with magnetic resonance imaging based measures of the anterior cingulate in 26 normal children ages 5 to 16 years. Attentional measures were assessed with a visual discrimination paradigm. Parasagittal slices from a 3-D, T1-weighted volume data set were used to obtain area measurements of the anterior cingulate. Response latencies decreased with age for both tasks. There were significant correlations between attentional performance and right, but not left, anterior cingulate measures. Performance was faster and more accurate during trials requiring predominantly controlled processes for those children with larger right anterior cingulate measures. The results are consistent with adult neuroimaging findings of activation in the right anterior cingulate during attention tasks and with lesion studies implicating greater right hemisphere involvement in attentional processes. © 1997 John Wiley & Sons, Inc. *Dev Psychobiol* **30**: 61–69, 1997

Keywords: cingulate; development; attention

The anterior cingulate cortex has been implied to play an essential role in initiation, motivation, and goal-directed behaviors. While this brain region has recently been further subdivided into “affect” and “cognitive” components (Devinsky, Mor-

rell, & Vogt, 1995), converging lines of evidence from animal, clinical, and neuroimaging studies suggest that the anterior cingulate cortex is centrally involved in controlling or directing our attention and actions by modulating cognitive (Goldman-Rakic, 1988; Mesalun, 1981; Posner, Petersen, Fox, & Raichle, 1988) and affective

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states (Ballantine, Bouckoms, Thomas, & Giriunas, 1987; Ballantine, Cassidy, Flanagan, & Marino, 1967; Meyer, McElhaney, Martin, & McGraw, 1973; Vogt, 1993; Vogt & Pandya). The current study examines the role of the anterior cingulate in the development of cognitive processes, specifically in attentional or controlled processing, during childhood.

Attentional processes are known to become more efficient with age (Casey, Rogers, & Fisk, 1987) across a time when brain size is not changing dramatically (Giedd, Snell, et al., 1996; Huttenlocher, 1979). Age-related differences in children's response latencies have been reported for a wide variety of tasks, ranging from simple reaction-time tasks to more complex cognitive tasks (e.g., Hale, 1990). The performance of these cognitive tasks generally involves the utilization of both automatic and attentional processes (Logan, 1985) where automatic processes refer to those which are data-driven, fast, operate in parallel, and are relatively effortless, whereas controlled or attentional processes are conceptually driven, relatively slow, serial, and require attentional resources. Most tasks are typically neither purely automatic nor controlled, but rather they are usually dominated by one or the other. However, it has been suggested that age-related differences in children's response latencies may be explained by age-related increases in the efficiency of attentional resources (Kail, 1986, 1988).

A number of positron emission tomography (PET) studies have provided support for the role of the anterior cingulate in attentional processes. For example, Pardo, Pardo, Janer, and Raichle (1990) reported the anterior cingulate gyrus was activated during the Stroop test (Stroop, 1935). This test assesses the susceptibility to interference from irrelevant stimuli. The task is to name the color in which color words are displayed. The interference that occurs is due to a tendency to read the word—an automatic response—as opposed to name the color. Pardo found activation of the right anterior cingulate with interference from the competing response (i.e., word reading as opposed to color naming) indicating that the right anterior cingulate may be involved in processing competing inputs and inhibiting competing actions.

Posner and colleagues (Posner, Petersen, Fox, & Raichle, 1988) demonstrated increases in blood flow in the anterior cingulate with increasing number of targets during a semantic decision task. When targets were rare—a paradigm used in vigilance assessment—blood flow changes were not as

great as when the number of targets were frequent. Pardo, Fox, and Raichle (1991) corroborated this finding with a lack of activation in the anterior cingulate during a visual and a somatosensory vigilance task. Thus, the cingulate cortex may not be involved in simple detection tasks, but rather in directing attentional responses when there are multiple or competing inputs and actions.

Similar findings were reported by Corbetta and colleagues (Corbetta, Miezin, Dobmeyer, Shulman, and Petersen, 1991) using a visual discrimination paradigm. They observed activation in the right anterior cingulate during detection of a change in a stimulus in any of three different features (shape, color, and speed), but not during detection of a change in only one of the three features. Thus, the right anterior cingulate appears to be involved more in attentional processing of competing inputs and less important in simple detection tasks.

To date, support for the role of the anterior cingulate in attentional processes has come exclusively from functional neuroimaging and clinical studies in adults. In children, functional neuroimaging has been problematic because activation studies to validate proposed structure–function relationships involve contrast agents or radiation exposure inherent in traditional neuroimaging techniques (e.g., PET, SPECT). This poses serious ethical issues when studying developmental populations. Nonetheless, it is important to understand attention developmentally as a key to both normal and neuropathological cognitive development. Thus, the use of noninvasive magnetic resonance imaging (MRI) to identify neuroanatomical correlates of attentional processes may further validate proposed structure–function relationships in the anterior attention system during development.

In the current study, we examined the role of the anterior cingulate in attentional tasks dominated by either controlled or automatic processes in children. A developmental neuroanatomical approach was taken to explore the role of the anterior cingulate in the development of attentional processes. Given that significant brain development (e.g., myelination, pruning, blood flow changes, etc.) continues throughout childhood and adolescence (Chugani, Phelps, & Mazziota, 1987; Huttenlocher, 1979) and at a time when attentional resources are assumed to become increasingly efficient, we hypothesized that these changes may be reflected in area measurements of specific brain regions of interest (e.g., the anterior cingulate). If so, then this normative data could be ap-

plied to the understanding of brain regions involved in psychopathologies characterized by attentional deficits. For the current study, we hypothesized that the size of the anterior cingulate, especially the right, would be related to performance of tasks dominated by controlled attentional processes, but not automatic processes.

METHODS

Subjects

Twenty-six normal volunteers (mean age = 10.5 years, $SD = 3.4$, range 5.3 to 16.4 years), 13 males and 13 females, were recruited from the local community. Assessment procedures included a physical and neurological examination, Child and Parent Diagnostic Interview for Children and Adolescents (Welner, Reich, Herjanic, Jung, & Amado, 1987), the Vocabulary and Block Design subtests of the Wechsler Intelligence Scale for Children—Revised (WISC-R) (Wechsler, 1981), and the 12 handedness items from the Physical and Neurological Examination for Subtle Signs (PANESS) inventory (Denkla, 1985). Two subjects were not administered the WISC-R subtests. All but one subject, a 16-year-old male, were right-handed. Individuals with physical, neurological, or lifetime history of psychiatric abnormalities or first-degree relatives with major psychiatric disorders such as schizophrenia, bipolar disorder, major depression, or mental retardation were excluded.

Behavioral Measurements

A modified version of the visual discrimination tasks used by Corbetta et al. (1991) were used to assess automatic and controlled attention. Subjects were given a forced-choice visual discrimination task (Casey, Gordon, Mannheim, & Rumsey, 1993; Casey, Vauss, & Swedo, 1994). Three stimuli were presented in a row on a computer screen (Figure 1). Stimulus presentation and response collection were all controlled by an IBM computer. The stimuli varied in shape (circle, triangle, or square) and in color (black or white). The subject's task was to determine which of the three stimuli was different from the other two. Subjects were not told which feature would be different. Subjects were instructed to respond as quickly as possible. The stimuli remained on the computer screen until the subject responded by pressing the 1, 2, or 3 button of a response box to indicate which of the

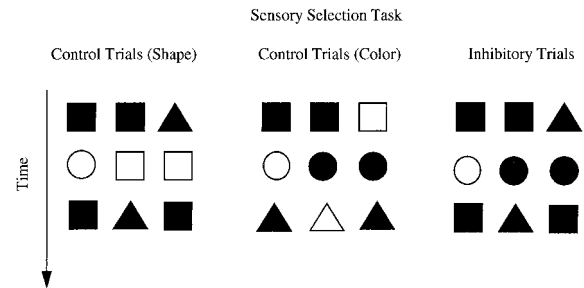


FIGURE 1 Illustration of trial types for the forced-choice visual discrimination task.

three shapes was different. Targets appeared equally often in each of the three locations in a random order.

In the predominantly automatic condition, the stimulus attribute on which the subject determined uniqueness was based on a single attribute (e.g., color), which was the same for a block of trials. Such forced-choice detections based on a single feature have been suggested to be relatively automatic (Treisman, 1986). In the controlled processing condition, the stimulus attribute changed from trial to trial within a block. Trials which are inconsistently mapped in this way and require shifts in attentional set from trial to trial have been suggested to require attentional resources or controlled processing (Shiffrin & Schneider, 1977). The subjects were presented with 36 trials per condition (72 total trials) and the conditions were counterbalanced. Five practice trials were given prior to testing to ensure that the subjects understood the task.

Anatomical Measurements

All subjects were scanned on a General Electric 1.5 Tesla Signa scanner located at the NIH clinical center. T1-weighted sagittal images with slice thickness of 1.5 mm using three-dimensional spoiled gradient recalled echo in the steady state (3-D SPGR) were obtained ($TE = 5$, $TR = 24$, flip angle = 45 degrees, acquisition matrix = 192×256 , $NEX = 1$, $FOV = 24$ cm). Head position was standardized by assuring that three external markers (vitamin E capsules in the meatus of each ear and one taped to the left inferior orbital ridge) were visible in the same axial reference plane. Foam padding was placed on both sides of the head to minimize head movement.

All scans were evaluated by a clinical neuroradiologist. No gross abnormalities were found in any

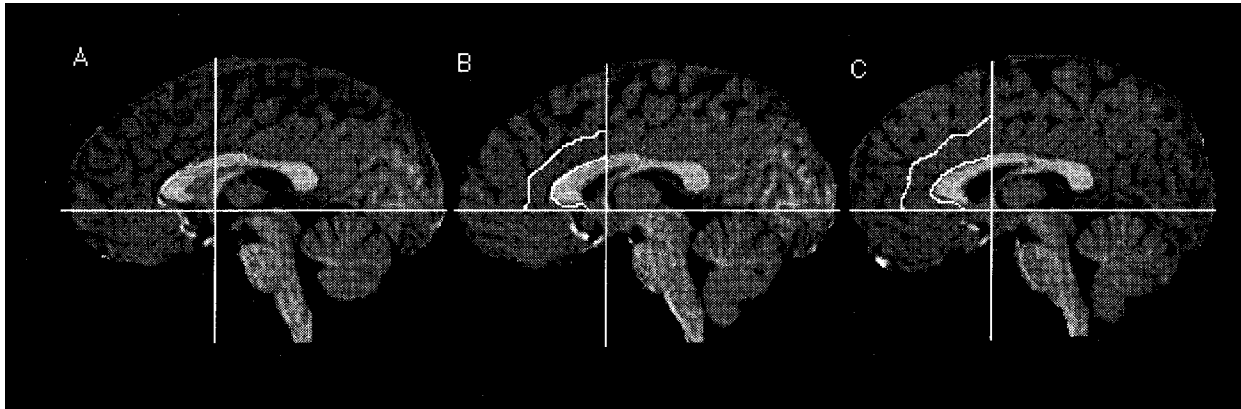


FIGURE 2 Panel A. The midsagittal slice identified by the septum pellucidum. Panel B depicts the boundaries for the anterior cingulate measure for a left parasagittal slice. Panel C depicts the boundaries for the anterior cingulate measure for a right parasagittal slice.

subjects. “Image,” an image analysis Macintosh software package (NIH Public Domain) (Rasband, 1993), was used to display the MRIs and quantify the regions of interest (ROIs). Anterior cingulate and cerebrum area measurements were obtained from parasagittal slices that were acquired 3 mm to the left and 3 mm to the right of the midsagittal slice. The midsagittal slice was defined by the presence of the septum pellucidum—the thin membrane that separates the frontal horns of the lateral ventricles (refer to Figure 2a). The boundaries of the left and right anterior cingulate region are depicted in Figure 2b and 2c, respectively. First, the classic intracommissural AC–PC line (line of anatomical reference between the anterior and posterior commissures) was identified on the midsagittal image. Then a line perpendicular to the AC–PC line was drawn through the anterior commissure (i.e., the AC vertical). This grid was overlaid onto the parasagittal slices located 3 mm to the left and 3 mm to the right of the midsagittal slice. The AC–PC line served as the inferior border of the cingulate region, while the AC-vertical served as the posterior border. This measure mainly consists of the “cognition” component (areas 24 prime and 32 prime) described by Devinsky, Morrell, and Vogt (1995) and consists less of areas 25 and 33 of the “affective” component of the anterior cingulate cortex. Area measurements of the cerebrum were taken from tracings on the same left and right parasagittal slices as the measurement of the anterior cingulate region.

Each region of interest was measured twice by an experienced rater who was blind to the subject’s age, sex, and behavioral performance. To establish

inter-rater reliability, ten subjects were selected at random and measured by a second experienced rater. The average interclass correlations for the interrater reliability were .94 and .90 for the anterior cingulate region and the cerebrum area measurements, respectively. Only the first rater’s data were used for this analysis. The average intraclass correlation for the intrarater reliabilities were .98 and .99, respectively. Efforts were made to obtain volumetric measures of the anterior cingulate gyrus from tracings of coronal images. However, reliability measures between raters fell below .70 so that area measurements were used because they correlated significantly with the volumetric measures (.91).

STATISTICAL ANALYSIS

Two-tailed *t* tests were performed to examine sex differences in age, estimated IQ based on two subtests of the WISC-R, attention measures (reaction times and accuracy on the automatic and controlled attention tasks), and MRI measures (left and right cerebrum and cingulate measures). A Bonferroni adjustment was made to correct for multiple comparisons, $p < .05/10 = .005$. Pearson correlations for MRI measures and attention measures with subject variables (age and estimated IQ) were calculated. Data from both male and female subjects were analyzed together in the correlational analysis given the relatively small sample size. Of most interest were partial correlations between the MRI and attention measures, correcting for age, IQ, and cerebrum size.

Table 1. Means and Standard Deviations of Attention and MRI Measures for all Subjects

	Total		Females		Males		
	<i>M</i>	(<i>SD</i>)	<i>M</i>	(<i>SD</i>)	<i>M</i>	(<i>SD</i>)	<i>t</i>
SUBJECT VARIABLES							
Age in months	125	(41)	124	(46)	126	(37)	−0.1
Estimated IQ (WISC-R)	128	(18)	119	(18)	137	(16)	−2.8
ATTENTION MEASURES							
Automatic Processes							
reaction time (ms)	1015	(421)	1081	(497)	947	(335)	0.8
accuracy rate	.98	(.03)	.97	(.04)	.98	(.01)	−1.4
Controlled Processes							
reaction time (ms)	1161	(627)	1303	(785)	1019	(398)	1.2
accuracy rate	.97	(.04)	.95	(.05)	.99	(.01)	−2.7
Controlled minus Automatic Difference							
Score (ms)	148	(310)	225	(406)	71	(150)	1.3
MRI MEASURES (mm ²)							
Right Cingulate Cortex	662	(238)	593	(231)	729	(236)	−1.5
Left Cingulate Cortex	769	(163)	774	(162)	764	(171)	−0.2
Cerebrum	22,097	(1749)	21,161	(1621)	23,032	(1361)	−3.2*

**p* < .005.

RESULTS

Sex Differences

Only cerebrum measurements were significantly larger for males relative to females (Table 1).

Developmental and Estimated IQ Correlates

As expected, response latencies for both predominantly automatic and controlled tasks correlated with age. However, only accuracy rate during the controlled task and not the automatic task was correlated with age. Furthermore, the right anterior cingulate measure was correlated with both age and estimated IQ (Table 2).

Neuroanatomical Correlates of Attention

Mean reaction times during the automatic and controlled processing tasks were negatively correlated with MRI area measurements of the right anterior cingulate region, but not with the left anterior cingulate region. These correlations have been plotted in Figure 3. Because age and estimated IQ were correlated with these measures, partial correlations correcting for these variables were performed. Furthermore, because variance in size of the anterior cingulate region may be due to differences in overall brain size, we controlled for overall size of the cerebrum. The results of this analysis are reported in Table 3. As shown, performance during the controlled task, but not

the automatic task, was faster and more accurate for children with larger area measures of the right anterior cingulate region. Furthermore, there was a significant negative correlation between the reaction time difference score of controlled versus automatic processing task performance and the right anterior cingulate measure. The larger the right anterior cingulate region, the smaller the difference between response latencies on these tasks.

DISCUSSION

This study examined the relationship between attentional measures and MRI measurements of the

Table 2. Pearson Correlations of Age and Estimated IQ with Attention and MRI Measures

	Subject Variables	
	Age in Months	Estimated IQ
ATTENTION MEASURES		
Automatic Processes		
reaction time (ms)	−.86**	−.26
accuracy rate	−.06	.21
Controlled Processes		
reaction time (ms)	−.77**	−.26
accuracy rate	.40*	.16
ANATOMICAL MEASURES		
Left Cingulate Cortex	.27	−.19
Right Cingulate Cortex	.39*	.42*
Cerebrum	.09	.27

p* < .05. *p* < .005.

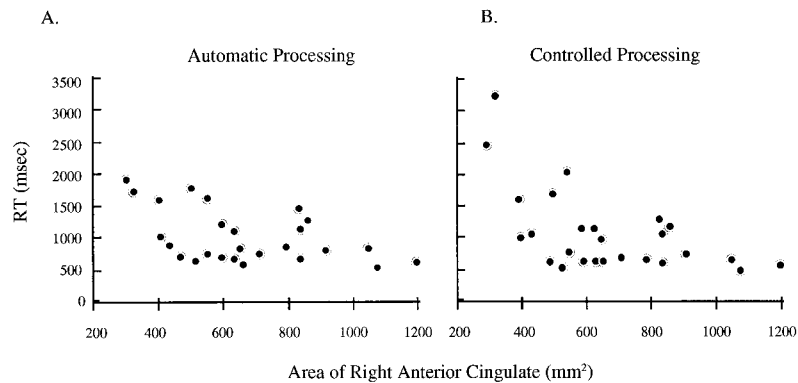


FIGURE 3 Panel A. A plot of response latencies during the predominately automatic processing task as a function of size of the right anterior cingulate. Panel B. A plot of response latencies during the predominately controlled processing task as function of size of the right anterior cingulate.

left and right anterior cingulate region in children. Attentional processes known to become more efficient with age were examined. First, age and attentional performance were correlated and as expected, the older children had faster response times on these tasks. Second, size of the right anterior cingulate region, but not the size of cerebrum, was correlated with age and estimated IQ. Third, while both mean response latencies and accuracy rates during the controlled processing task correlated with the right anterior cingulate measurement, neither correlated with the left anterior cingulate measurement. Fourth, only the controlled task performance, and not the automatic task performance, appeared to be related to the area measurement of the right anterior cingulate region

after controlling for age, estimated IQ, and size of the cerebral cortex. This relationship was further reflected in a difference score that was calculated by subtracting reaction times during performance of the more automatic task from the controlled task, which also correlated with the right anterior cingulate measure.

The finding of faster reaction times as a function of age is consistent with the cognitive developmental literature. These age-related differences in children's response latencies have been reported for a wide variety of simple and complex tasks (Hale, 1990). While our results do not provide direct support for the hypothesis that age-related differences in children's response latencies are due to age-related increases in attentional resources (Kail, 1986, 1988), our results are consistent with this view. Because the performance of most cognitive tasks typically involves the utilization of both automatic and attentional processes and typically is neither purely automatic nor controlled (Logan, 1985), this may explain the age-related decrease in response times for both of our tasks.

The correlation between the size of the right anterior cingulate region and age, but not cerebrum and age, may be explained by the parasagittal slices being most representative of the cingulate gyrus, and not the cerebrum. However, there now appears to be converging evidence that total brain mass levels off by age 5 (Giedd, Snell, et al., 1996; Jernigan, Trauner, Hesselink, & Tallal, 1991; Kretschmann, Kammrad, Krauthausen, Sauer, & Wingert, 1986; Pfefferbaum et al., 1994). The significant correlation between age and anterior cingulate cortex may correspond to a differential increase in growth in this area that corresponds with

Table 3. Partial Correlations of MRI Measures with Attention Measures Controlling for Age, IQ, and Size of Cerebral Cortex

Attention Measures	MRI Measures	
	Right Anterior Cingulate Cortex	Left Anterior Cingulate Cortex
AUTOMATIC PROCESSES		
Reaction Time	.17	-.13
Accuracy Rate	.01	.27
CONTROLLED PROCESSES		
Reaction Time	-.45*	-.32
Accuracy Rate	.49**	.34
CONTROLLED MINUS AUTOMATIC Difference Score		
	-.48*	-.33

* $p < .05$. ** $p < .01$.

increased attentional capacity. Alternatively, this increase in the right anterior cingulate cortex may correspond to a more generalized increase in growth of the right hemisphere. This explanation is supported by reports of other right-hemisphere brain regions showing linear increases across the same age range (e.g., Giedd, Vaituzis, et al., 1996). Our results should be replicated using reliable volumetric measures and large sample sizes similar to those reported by Paus et al. (1996) before further interpretation can be made.

Our results are consistent with PET blood-flow studies showing right and not left cingulate activity to be correlated with performance on tasks requiring a high demand for attention (Corbetta et al., 1991; Pardo et al., 1990). While both mean response latencies and accuracy rates during the predominantly controlled processing task correlated with the right anterior cingulate measurement, neither correlated with the left anterior cingulate region.¹ Our controlled processing task incorporated task components of both Corbetta's "divided" attention task (e.g., processing several stimulus attributes simultaneously) and the Stroop task (i.e., inhibiting response tendency to read the word), both of which resulted in robust PET activation of the right anterior cingulate gyrus (Corbetta et al., 1991, Stroop, 1935). In our task, the subject had to both process multiple stimulus attributes (shape and color) and inhibit attentional responses to the irrelevant attributes (e.g., inhibit attention to attributes important for the previous trial, but not the current trial). These data are consistent with a role of the right anterior cingulate gyrus in processing competing inputs and inhibiting or suppressing competing responses.

Why would the size of the cingulate affect attentional processes? One hypothesis is that greater myelination in this area may result in more efficient processing between regions within a functional network. The cingulate cortex does not function in isolation. The observed projections from both the posterior parietal and dorsolateral prefrontal cortex (Goldman-Rakic, 1988) suggest that this structure may play a large role in the regulation of cognitive activity, especially in processing competing inputs and inhibiting competing responses to these inputs. Thus, greater myelination of projections from these structures may explain the increase in size of the cingulate cortex with age as well as the faster reaction times (i.e., increased efficiency) on the attentional tasks. Other possible explanations may include an increase in dendritic connections in this region as

well as in support cells. These explanations are only speculative and our results should be replicated before further interpretation can be made.

Finally, the larger size of the cerebrum in males for this sample is consistent with both autopsy (Blinkov & Glezer, 1968; Ho, Roessmann, Straumfjord, & Monroe, 1980) and imaging studies (Andreasen et al., 1993; Filipek, Richelme, Kennedy, & Caviness, 1994; Pfefferbaum et al., 1994; Shultz et al., 1994). Given the multiple parameters determining overall brain size, a larger brain size should not be interpreted as imparting functional advantage or disadvantage.

In sum, additional insight into the role of the anterior cingulate cortex in attentional processing in children may be gained by studying regions projecting to and from this area (e.g., posterior parietal and dorsolateral prefrontal cortex). Unfortunately, defining boundaries for these regions are somewhat more ambiguous than those of the anterior cingulate gyrus. Nevertheless, these brain regions should be considered in developmental populations (both normal and pathological). Another possible approach will be the use of the recently developed technique of noncontrast functional MRI (Kwong et al., 1992; Ogawa et al., 1992). This technique records changes in blood flow and oxygenation state of brain tissue thereby indexing brain activation. Because functional MRI is noninvasive, it can be used to study structure/function relations in pediatric populations more directly. We have recently had success in applying this methodology to pediatric populations (Casey et al., 1995a; Casey et al., 1995b). It is our hope to further examine the role of the anterior cingulate cortex in additional processes of children and developmental psychiatric patients with this technique in the near future.

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